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Synthesis and characterisation of aluminium (III) imine bis(phenolate) complexes with application for the polymerisation of *rac*-LA

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A series of tridentate imine bis(phenolate) ligands have been synthesised and complexed to aluminium. Solid-state analysis identified two structural motifs of an aluminium dimer $[Al_2(Me)_2(\mathbf{X})_2]$; one consisting of two five-coordinate aluminium centres and a second containing aluminium centres in both a six- and four-coordinate geometry. Pairing with solution-state NMR spectroscopic analysis suggested that the geometry isolated was influenced by the ligands' steric bulk. Trialling of $Al_2(Me)_2(\mathbf{1}\text{-}\mathbf{5})_2$ as initiators for the ring-opening polymerisation (ROP) of *rac*-lactide found them all to be active, producing atactic polymeric material. $Al_2(Me)_2(\mathbf{1})_2$ was found to have good molecular weight control and activity an order of magnitude higher than analogous aluminium dimers.

Introduction

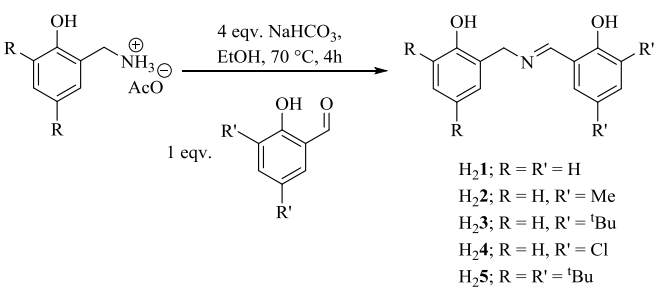
The quest for improved renewable plastics continues to be prevalent in the literature; whether that be in the form of new bio-based materials or through the controlled synthesis of existing bio-based polymers to provide enhanced properties and widen subsequent potential applications.[1] Polylactide (PLA) is one such bio-based polymer and, with a monomer unit consisting of a cyclic dimer of lactic acid, can be both renewably resourced and biodegraded (under adequate conditions) at the end of its life.[2, 3] Polylactide is also biocompatible and thus is attractive for both commodity and high-value biomedical applications.[4] PLA can be produced through the controlled ring-opening polymerisation (ROP) of lactide, facilitated through the use of a Lewis acid metal-ligand complex.[5] In the presence of either a labile alkoxide or alcohol as a co-initiator, a wide range of metal complex have been reported as active for the ROP of lactide, with varying degrees of molecular weight and stereochemical control.[6-15]

Tridentate ligand systems with phenolate, amine or imine functionality have been widely reported, with the accessibility of a number of substituted anilines providing a route to studying the effect of phenolate substituents on ROP activity.[10, 16-18] Imine functionality is more rigid than the corresponding amine and it has been suggested is important for isotactic stereochemical control.[19, 20] A series of salalen ligands previously reported offered both rigid imine and more flexible amine functionality in the form of a tetradentate ligand.[21] In this work we present a family of imine bis(phenolate) ligands that incorporates a methylene linker for increased flexibility, compared to its aniline-derived analogues, whilst maintaining a tridentate binding potential Surprisingly, examples of these simple ligands based on methylene linked imines are rare in the literature compared to their aniline derived cousins.[22-24] These ligands were coordinated to $AlMe_3$, the complexes characterised in the solid (single-crystal XRD) and solution (NMR) state, and then trialled as initiators for the ROP of *rac*-lactide.

Results and Discussion

Metal Complex Synthesis

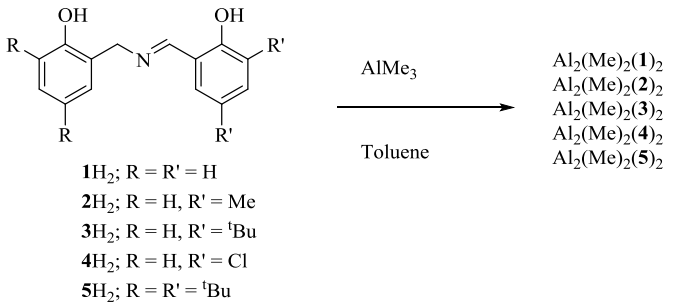
The imine bis(phenolate)pro-ligands ($H_2\mathbf{1}$-$\mathbf{5}$) were synthesised *via* an imine condensation reaction between a 3,5-substituted salicyaldehyde and salicylamine, that was generated *in-situ* from a salicylammonium acetate, Scheme 1:



Scheme 1. Synthesis of substituted imine bis(phenolate)pro-ligands $H_2\mathbf{1}$-$\mathbf{5}$

Structures of ligands $H_2\mathbf{1}$, $H_2\mathbf{2}$, $H_2\mathbf{4}$ and $H_2\mathbf{5}$ were determined by single-crystal X-ray diffraction.† Coordination to trimethyl

aluminium was carried out in toluene at ambient temperature using standard Schlenk line techniques, Scheme 2.†



1H_2; R = R' = H
2H_2; R = H, R' = Me
3H_2; R = H, R' = ^{t}Bu
4H_2; R = H, R' = Cl
5H_2; R = R' = ^{t}Bu

Scheme 2. Synthesis of aluminium(III) imine bis(phenolate) complexes $Al_2(Me)_2$(**X**)$_2$

Complex characterisation

The solid-state structures for $Al_2(Me)_2$(**2**)$_2$, $Al_2(Me)_2$(**4**)$_2$ and $A_2(Me)_2$(**5**)$_2$ were determined, identifying two structural motifs of an aluminium-ligand dimer. $Al_2(Me)_2$(**2**)$_2$ and $Al_2(Me)_2$(**5**)$_2$ were found to contain of a four-coordinate and six-coordinate aluminium, whilst $Al_2(Me)_2$(**4**)$_2$ was found to contain two five-coordinate, pseudo-bipyramidal aluminium centres, Figure 1. In both structural motifs, bridging was facilitated by the oxygen centre from the more flexible methylene-bridged phenolate.

Comparison of the ^{1}H NMR spectra of $Al_2(Me)_2$(**1**)$_2$ and $Al_2(Me)_2$(**3**)$_2$ with that of $Al_2(Me)_2$(**2**)$_2$, $Al_2(Me)_2$(**4**)$_2$ and $Al_2(Me)_2$(**5**)$_2$ suggested that similar motifs were present and that steric bulk of the ligand influenced the resulting structural motif. To that end it is concluded that $Al_2(Me)_2$(**1**)$_2$ and $Al_2(Me)_2$(**4**)$_2$ exist in the dual five-coordinate motif (5°-5°) whilst $Al_2(Me)_2$(**3**)$_2$ and $Al_2(Me)_2$(**4**)$_2$ exist as the six- and four-coordinate structural motif (6°-4°), Figure 2. Analysis of the solution state NMR spectrum of $Al_2(Me)_2$(**2**)$_2$, which can be deemed to have a ligand of intermediate steric bulk in the series, displays resonances which are tentatively attributed to both structural motifs, Figure S1.†

To further explore the relationship between ligand steric bulk and dimer structural motif, $Al_2(Me)_2$(**2**)$_2$ was synthesised at two concentrations of ligand (0.1 M and 0.2 M) to discern if ligand concentration had an effect on structural motif. At these concentrations it was found that there was no effect on the structure; based on solution state ^{1}H NMR spectra, Figure S2.† Analysis of the ^{1}H NMR spectrum of $Al_2(Me)_2$(**4**)$_2$ identified two sets of imine peaks (8.0 – 8.5 ppm) and two pairs of doublets for the diastereotopic methylene bridge protons. It is tentatively proposed that this is due to the presence of two isomers of the 5°-5° structural motif. The 'cis' isomer, with the two methyl groups on the same side of the dimer, is found in the solid-state *via* single-crystal X-ray diffraction, whilst the 'trans' is proposed, Figure 3.

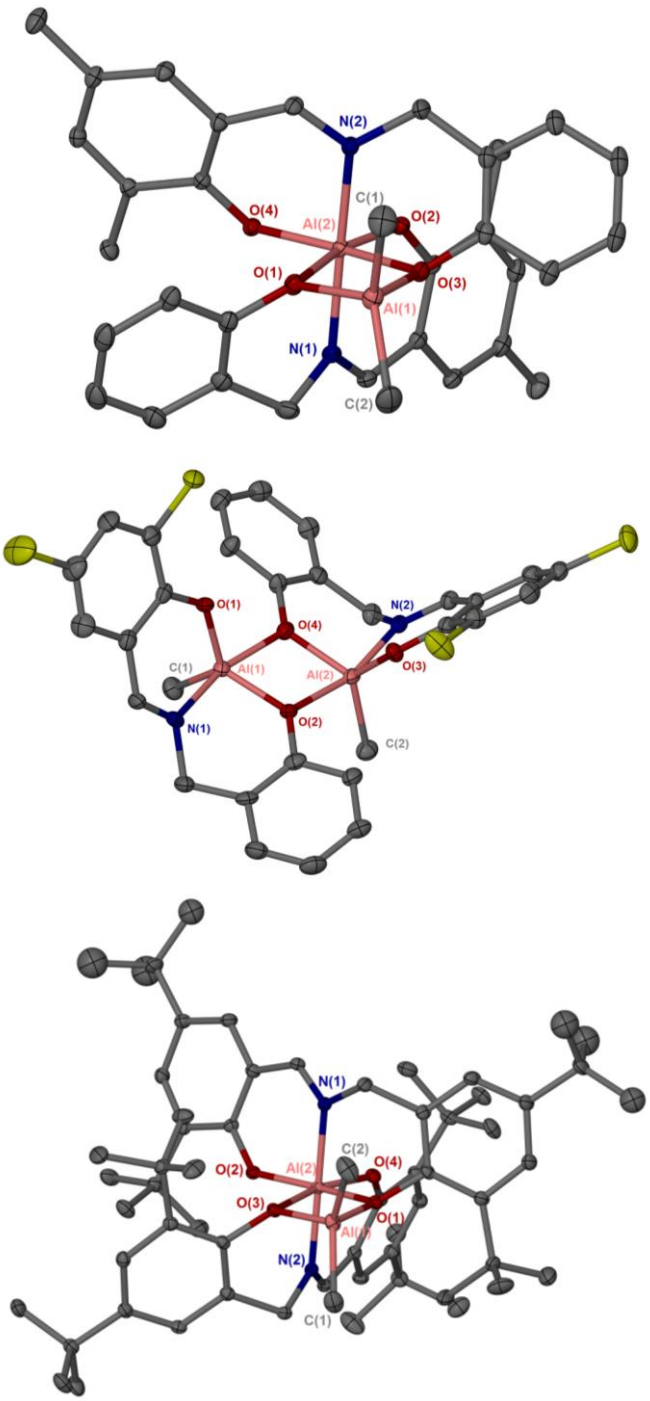


Figure 1. Solid-state structure of $Al_2(Me)_2$(**2**)$_2$ (top), $Al_2(Me)_2$(**4**)$_2$ (middle) and $Al_2(Me)_2$(**5**)$_2$ (bottom) as determined by single-crystal X-ray diffraction. Ellipsoids are shown at the 30% probability level. All disorder and hydrogen atoms have been removed for clarity. See supporting information for bond lengths and angles.

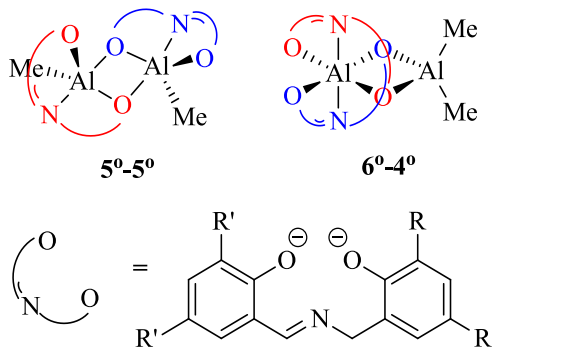


Figure 2 Two dimeric structural motifs identified in the solid-state by single-crystal X-ray diffraction.

In an attempt to probe the possibility of a 'trans' isomer being present, DFT calculations were carried out to determine the free energies of the 'cis' and 'trans' isomers of $Al_2(Me)_2$(**4**)$_2$. Crystallographic data provided the input coordinates for the 'cis' isomer and this was manipulated to generate the 'trans' isomer, Figure 3. Optimisation was carried out using the following protocol: rwb97xd / 6-13g(d,p) / scrf= (cpcm, solvent = toluene). Free energies for the optimised 5°-5° 'cis' isomer and 5°-5° 'trans' isomer were found with the 'cis' isomer more favourable by 0.51 kcal mol^{-1}. Such an energy difference is not significant and based on this initial calculation, using the basis set stated, the 'cis' and 'trans' isomers are not thermodynamically distinguishable and thus both possible. Furthermore, the order of addition (ligand to metal or metal to ligand) had little effect on the product distribution.†

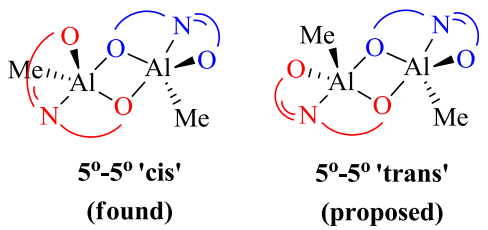


Figure 3. Isomers of the dimeric aluminium complex – 'cis' as derived from solid-state X-ray diffraction data and a proposed 'trans' isomer.

Lactide Polymerisation Trials

$Al_2(Me)_2$(**1-5**)$_2$ were trialled as initiators for the ROP of *rac*-lactide in the presence of benzyl alcohol (BnOH) as a co-initiator. Polymerisations were carried out in toluene at 353 K with [LA] = 0.8 M and [LA]:[I]:[BnOH] = 100:1:1. Ratios were calculated "per metal centre", Table 1:

Table 1. ROP of *rac*-lactide initiated by BnOH and $Al_2(Me)_2$(**1-5**)$_2$

Initiator	Conv. /% [d]	M_n^{calc}	M_n [e]	PDI [e]	P_r [f]
$Al_2(Me)_2$(**1**)$_2$ [a]	99	7250	11450	1.49	0.47
$Al_2(Me)_2$(**1**)$_2$ [b]	97	14100	24250	1.41	0.53
$Al_2(Me)_2$(**1**)$_2$ [c]	98	28350	51525	1.28	0.51
$Al_2(Me)_2$(**2**)$_2$ [b]	97	14100	11800	1.19	0.47
$Al_2(Me)_2$(**3**)$_2$ [b]	95	13800	10300	1.22	0.56
$Al_2(Me)_2$(**4**)$_2$ [b]	99	14350	13050	1.32	0.45
$Al_2(Me)_2$(**5**)$_2$ [a]	99	7250	9975	1.20	0.54
$Al_2(Me)_2$(**5**)$_2$ [b]	90	13050	21125	1.07	0.55

Reaction conditions: toluene, T = 353 K, reaction time = 24 h, [LA]:[I]:[BnOH] = [a] 50:1:1, [b] 100:1:1, [c] 200:1:1. [d] Determined *via* ^{1}H NMR. [e] Determined from GPC (in THF) referenced to polystyrene standards. [f] Calculated from ^{1}H homonuclear decoupled NMR ($CDCl_3$) analysis. The calculated molecular weights were determined by the following (Eq. LA × 144 × conversion/100) + 108 {where 108 is the mass of the end groups (H/OCH_2Ph)}.

All complexes were found to be active for the ROP of *rac*-lactide, producing polymeric material of an atactic nature. Molecular weights were comparable for $Al_2(Me)_2$(**2-4**)$_2$ however, measured molecular weights were considerably higher for $Al_2(Me)_2$(**1**)$_2$ and $Al_2(Me)_2$(**5**)$_2$. Polydispersity was found to be higher for complexes with the less sterically hindered ligands $Al_2(Me)_2$(**1**)$_2$ and $Al_2(Me)_2$(**4**)$_2$; with less steric bulk about the metal centre the propensity of transesterification during propagation is greater. The apparent reduced molecular weight control may be due to complications with the formation of a ROP-active species for the 6°-4° structural motif. Due to the reactive nature of the aluminium-methyl bond it is proposed that an alkoxide species is generated *in situ* prior to the coordination and insertion of the first lactide unit. With respect to $Al_2(Me)_2$(**1**)$_2$, ^{1}H NMR spectroscopic studies in d_8-THF showed that potentially one of the proposed 5°-5° isomers is undisturbed by a coordinative solvent, (Figure S4).† In a coordination-insertion mechanism for the ROP of lactide the lack of disruption to the dimer may suggest catalytic inactivity for one of the proposed isomers.

Further investigation of the activity $Al_2(Me)_2$(**1**)$_2$ was carried out through varying the initiator loading. Polymerisations with a [LA]:[I]:[BnOH] of 50:1:1 and 200:1:1 were carried out yielding polymeric material with number-average molecular weights (M_n) of 11450 and 51525 g/mol respectively. As with the initial polymerisation trial, molecular weights were higher than expected based on a "per-metal-centre" loading, however a controlled molecular weight change was observed with altering initiator loading. This provides evidence that $Al_2(Me)_2$(**1**)$_2$ is exhibiting relative predictable molecular weight control.

Reaction time for the ROP of *rac*-lactide using $Al_2(Me)_2$(**1**)$_2$ was reduced to six hours with no discernible impact on conversion (97 %) or polymer molecular weight (M_n = 24250). PDI was significantly reduced (from 1.41 to 1.10) suggesting that the longer reaction time provided greater opportunity for transesterification. However, it should be noted that both

reaction times produced atactic polymeric material suggesting the lack of stereoselectivity is inherent to the initiator rather than due to excessive transesterification.

Polymerisation Kinetics

Kinetics studies were carried out for the ROP of lactide using $Al_2(Me)_2(\mathbf{1})_2$ in d_8-toluene at 353 K, with conversion monitored *in situ* using ^{1}H NMR spectroscopy. Studies of both *rac*-lactide and L-lactide were found to be pseudo-first order, with a semi-ln graph of $\ln\left(\frac{[LA]_0}{[LA]_t}\right)$ versus *t* providing a straight line where the gradient was equal to the apparent rate constant (k_{app}), Figures 4 and 5. Apparent rate constants for the ROP of *rac*-lactide and L-lactide were found to be 1.30×10^{-2} min^{-1} and 1.41×10^{-2} min^{-1} respectively. These aluminium dimers are comparable to previously reported half-salen complexes.[10] The similarity in apparent rate constants for both the racemic and enantio-pure lactide further confirms the non-stereoselective nature of $Al_2(Me)_2(\mathbf{1})_2$. This lack of selectivity can be quantified by the applying the apparent rate constants in the following equation, as applied previously in the literature: $P_r = 1 - \frac{1}{2}\left(\frac{k_{(L-L)}}{k_{(rac)}}\right)$, where $k_{(rac)}$ and $k_{(L\text{-}L)}$ are the apparent rate constants for the ROP of *rac*-lactide and L-lactide respectively.[25] For $Al_2(Me)_2(\mathbf{1})_2$ the kinetic derived P_r = 0.46, which is comparable to that measured *via* homonuclear decoupled ^{1}H NMR spectroscopy.

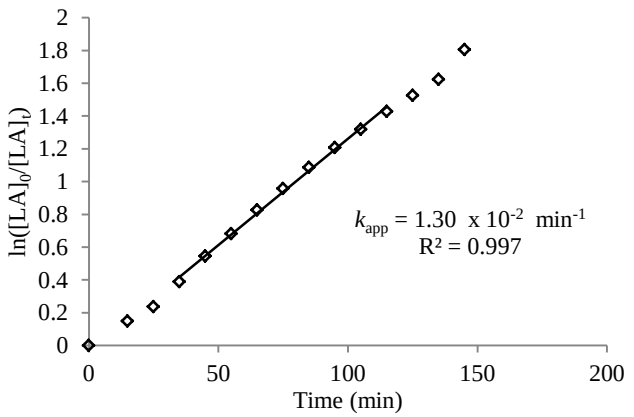


Figure 4. Semi-ln plot for the ROP of *rac*-lactide by $Al_2(Me)_2(\mathbf{1})_2$ showing pseudo-first order kinetics. [LA] = 0.8 mol dm^{-3}, [LA]:[I]:[BnOH] = 100:1:1, 353 K, toluene-d_8

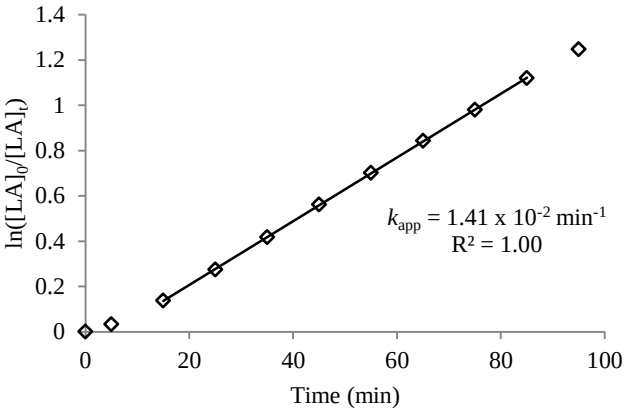


Figure 5. Semi-ln plot for the ROP of L-lactide by $Al_2(Me)_2(\mathbf{1})_2$ showing pseudo-first order kinetics. [LA] = 0.8 mol dm^{-3}, [LA]:[I]:[BnOH] = 100:1:1, 353 K, toluene-d_8

Conclusions

A range of dimeric aluminium imine bis(phenolate) have been synthesised and demonstrated two structural motifs; deemed to be dependent on the steric bulk of the imine bis(phenolate) ligand. Ligands with less steric bulk tended to a 5°-5° dimer whilst those with larger substituents adopting a 6°-4° dimer motif that facilitated greater spacial distribution of the bulky phenolate rings. Complexes with ligands consisting of intermediate steric bulk were found to contain both binding motifs in the crude form. All complexes were found to be active for the ROP of *rac*-lactide with no induced stereoselectivity and producing atactic polymeric material with $Al_2(Me)_2(\mathbf{1})_2$ showing relatively good molecular weight control. Work is on-going to investigate the solution behaviour of the complexes in more detail.

Experimental

Trimethylaluminium (2M in hexane, Aldrich) was used as supplied. All other starting materials were used as received from either Sigma Aldrich or TCI, Ltd. *rac*-lactide (Aldrich) was recrystallized from dry toluene and sublimed twice prior to use in polymerisation reactions. Preparation of all metal complexes and subsequent ROP of *rac*-lactide were performed under an inert atmosphere of argon using standard Schlenk or glove-box techniques. All solvents used in the preparation of metal complexes were dry and obtained via an SPS (Solvent Purification System). Full analysis is given in the supporting information.

A representative synthesis of ligand $H_2\mathbf{1}$ is given:

Salicylammonium acetate (2.00 g, 10.9 mmol) and sodium bicarbonate (3.67 g, 43.7 mmol) were mixed with ethanol (100 ml) and heated to 60° C. Salicylaldehyde (1.33 g, 10.9 mmol) was added drop-wise to the reaction mixture and left to stir for 2 hours. The reaction mixture was then hot filtered and washed with hot ethanol to remove insoluble salts. Solvent was

removed and the resulting yellow solid washed with distilled water to remove any soluble sodium salts. The disalicylaldimine, a yellow solid, was washed with hexane to remove unreacted aldehyde and dried under high vacuum (1.68 g, 7.39 mmol, 68%). ^{1}H NMR (d_6-DMSO) 4.73 (2H, s, $PhCH_2N$), 6.85 (4H, m, Ar-H), 7.15 (2H, m, Ar-H), 7.32 (1H, td J = 7.5, 0.9 Hz, Ar-H), 7.45 (1H, dd J = 0.9, 7.5 Hz, Ar-H), 8.63 (1H, s, CH=N), 9.65 (1H, bs, OH), 13.72 (1H, bs, OH). $^{13}C\{^1H\}$ NMR (d_6-DMSO) 57.03 (CH_2N=C), 115.1, 116.5, 118.4, 118.6, 119.0, 124.4, 128.5, 129.3, 131.6, 132.3 (Ar-CH), 155.2 (Ar-O), 160.9 (CH=N), 166.1 (Ar-O). m/z calc. $[C_{14}H_{13}NO_2+Na]^+$ = 250.0844, found 250.0831.

Complexes:

Imine bis(phenolate) complexation was carried out on a 0.5 g scale. The ligand H_2(**1-5**) was charged to a Schlenk flask and placed under an inert atmosphere. Dry toluene (~10 ml) was added to the flask *via* a cannula before the addition of 1 equivalent of $AlMe_3$ (2 M in hexane). The reaction was stirred at room temperature for 1 hour before the removal of solvent under reduced pressure to yield a yellow solid. Crude material was recrystallised in hot toluene.
Representative analysis for $Al_2(Me)_2$(**1**)$_2$ ^{1}H NMR (C_6D_6) -0.03 (6H, s, Al-CH_3), 3.53 (2H, d (J = 14.0 Hz), CH_2-N), 5.30 (2H, d (J = 14.0 Hz), CH_2-N), 6.64 (2H, dd (J = 1.0, 6.9 Hz), Ar-H), 6.74 (2H, dd (J = 1.7, 7.7 Hz), Ar-H), 6.94 (2H, dt (J = 1.6, 7.5 Hz), Ar-H), 6.99-7.05 (4H, m, Ar-H), 7.12 (2H, dd (J = 1.9, 6.9 Hz), Ar-H), 7.29 (2H, s, CH=N), 7.37 (2H, dt (J = 1.7, 7.9 Hz), Ar-H), 8.41 (2H, dd (J = 0.7, 8.5 Hz), Ar-H). $^{13}C\{^1H\}$ NMR (C_6D_6) -8.10 (Al-*C*H_3), 60.8 (N-*C*H_2), 117.3, 119.9, 121.1, 122.1, 122.8, 126.3, 128.2, 129.0, 133.3, 135.4 (Ar-*C*), 154.4 (*C*H=N), 164.0, 165.2 (Ar-O). Anal: calc. for $C_{15}H_{14}NO_2Al$: C, 67.4; H, 5.28; N, 5.24. Found: C, 66.7; H, 5.27; N, 4.72.

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Notes and references.

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† ESI available: [Full characterisation and experimental procedures]. See DOI: 10.1039/b000000x/

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